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Combination Eravacycline Therapy for Carbapenem-Resistant *Acinetobacter baumannii* Pneumonia

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BACKGROUND

- *Acinetobacter baumannii* predominately causes pneumonia and bloodstream infections in debilitated, hospitalized patients[1]
- Multiple virulence factors and antibiotic resistance mechanisms leading to frequent isolation of multi-drug resistant (MDR) phenotypes, such as carbapenem-resistance *Acinetobacter baumannii* (CRAB), make treatment difficult[2]
- Combination salvage therapy for CRAB often used despite limited evidence showing clinical superiority over monotherapy[3]
- Eravacycline has greater *in-vitro* potency against MDR *A. baumannii* compared to tigecycline, but lack of clinical evidence to support efficacy has limited its use for this indication[4,5]

PURPOSE

Primary Outcome: Clinical resolution of CRAB pneumonia

- Intended course of therapy completed
- Therapy ≤ 14 days
- Therapy not restarted within 48 hours of discontinuation

Secondary Outcomes:

- Microbiological resolution
- Incidence of patients requiring > 14 days of therapy
- Incidence of patients restarting eravacycline therapy within 48 hours of discontinuation

METHODS

Retrospective case series, April 1st to October 1st, 2020

Inclusion Criteria

- Adults ≥ 18 years of age
- Positive SARS-CoV-2 molecular test
- Respiratory culture positive for CRAB
- Clinical diagnosis of new bacterial pneumonia
- Receipt of ≥ 1 dose of eravacycline

Exclusion Criteria

- CRAB bacteremia

RESULTS

Patient Characteristics (N=25)	
Median age, years (range)	53 (32 – 77)
Male sex, n (%)	16 (64)
Mechanical ventilation at time of culture, n (%)	25 (100)
Body mass index (BMI), n (%)	
Overweight (BMI: 25.0 – 29.9)	6 (24)
Class 1 obesity (BMI: 30.0 – 34.9)	7 (28)
Class 2 obesity (BMI: 35.0 – 39.9)	4 (16)
Severe obesity (BMI: ≥ 40.0)	8 (32)
Comorbidities, n (%)	
Hypertension	16 (64)
Diabetes mellitus	14 (56)
Active immunosuppressive agents prior to admission	2 (8)
Chronic lung disease	1 (4)
Chronic kidney disease	1 (4)
Chronic liver disease	1 (4)
Hematologic malignancy	1 (4)
HIV/AIDS (CD4 < 200 cells/µL)	0 (0)
Neutropenia (ANC < 500 cells/µL)	0 (0)
Median time from admission to MV, days (range)	9 (0-18)
Polymicrobial culture, n (%)	19 (76)
Combination Therapy, n (%)	
Eravacycline + ampicillin-sulbactam	17 (68)
Eravacycline + ampicillin sulbactam + inhaled colistin	7 (28)
Eravacycline + inhaled colistin	1 (4)

In-vitro susceptibilities for CRAB isolates				
Antibiotic*	Susceptibility rate, n (%)			
	Susceptible	Intermediate	Resistant	Not reported
Ampicillin-sulbactam	15 (60)	9 (36)	1 (4)	0 (0)
Colistin	---	20 (80)	1 (4)	4 (16)
Cefepime	0 (0)	1 (4)	18 (72)	6 (24)

*All isolates were resistant to meropenem, ciprofloxacin, gentamicin, tobramycin, and TMP-SMX

Tigecycline Minimum Inhibitory Concentration (MIC)				
MIC	0.25	0.5	1	Not reported
Number of isolates, n (%)	12 (48)	8 (32)	0 (0)	5 (20)

Primary and Secondary Outcomes (N=25)	
Primary Outcome	
Clinical Resolution, n (%)	18 (72)
Secondary Outcomes	
Microbiological resolution, n/N* (%)	13/18 (72)
Median duration of therapy, n (range)	10 (1-27)
Received greater than 14 days of therapy	1 (4)
Restarted therapy within 48 hours of initial discontinuation	0 (0)

LIMITATIONS

- Retrospective design
- Small sample size
- Co-infected with SARS-CoV-2
- Further studies needed to determine eravacycline efficacy

CONCLUSION

- Recently published guidance on the treatment of antimicrobial-resistant gram-negative infections does not suggest eravacycline for the treatment of CRAB infections, due to lack of clinical data[5]
- In this case series, combination therapy with eravacycline demonstrated favorable clinical and microbiological outcomes
- In light of limited treatment options, eravacycline is another agent that can be considered for CRAB pneumonia salvage therapy

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